Histologic examination

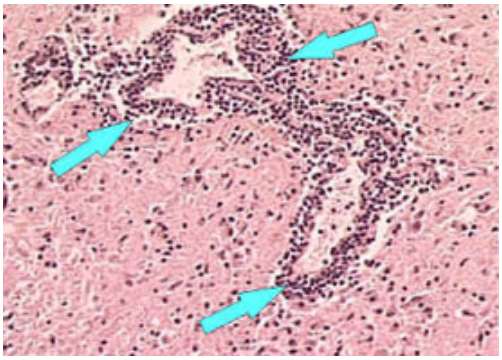
General histopathology

Histologic examination of biopsy or autopsy tissues is occasionally useful in diagnosing unsuspected cases of rabies that have not been tested by routine methods. When brain tissue from rabies virus-infected animals are stained with a histologic stain, such as hematoxylin and eosin, evidence of encephalomyelitis may be recognized by a trained microscopist. This method is nonspecific and not considered diagnostic for rabies.

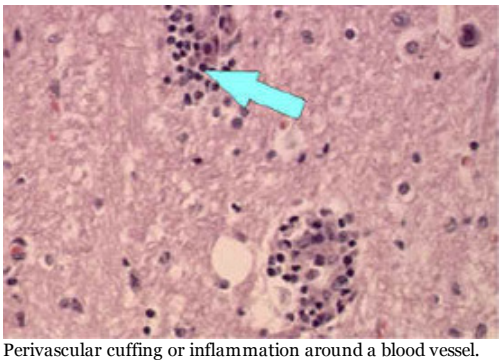
Before current diagnostic methods were available, rabies diagnosis was made using this method and the clinical case history. In fact, most of the significant histopathologic features (changes in tissue caused by disease) of rabies infection were described in the last quarter of the 19th century. After Louis Pasteur's successful experiments with rabies vaccination, scientists were motivated to identify the pathologic lesions of rabies virus.

Histopathologic evidence of rabies encephalomyelitis (inflammation) in brain tissue and meninges includes the following:

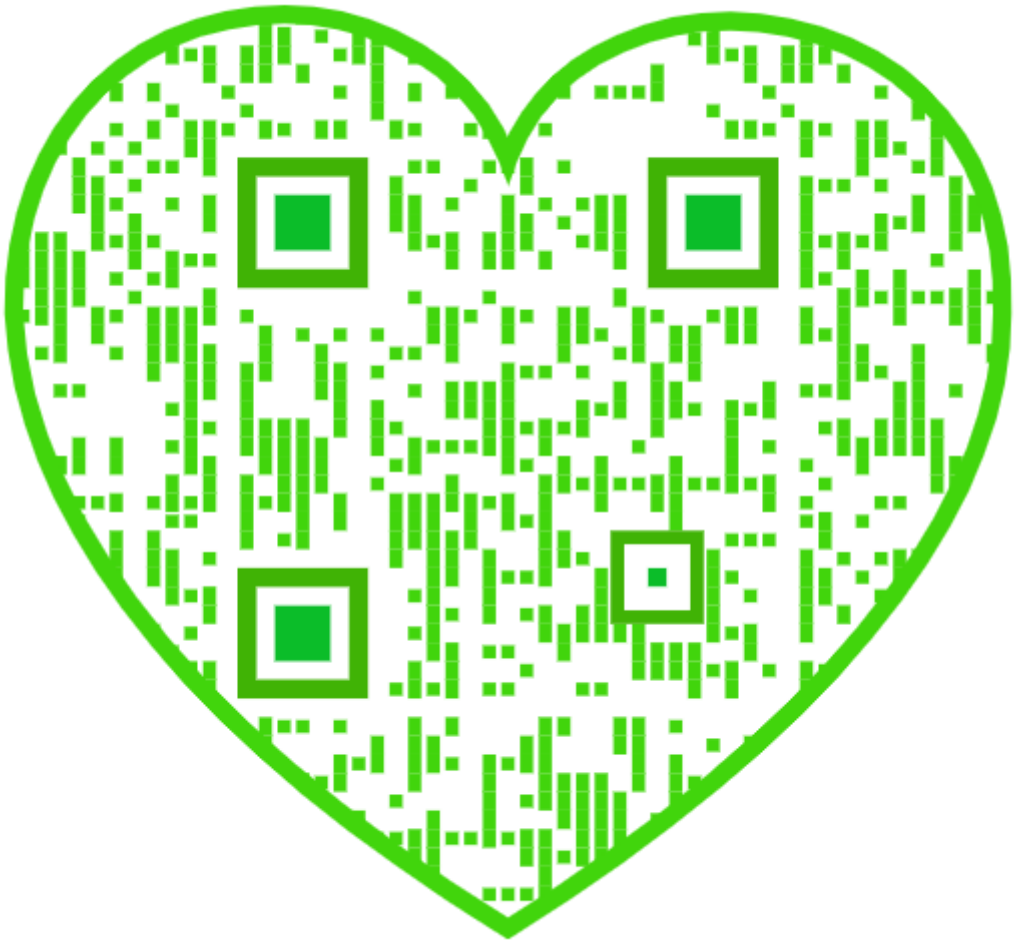
1. Mononuclear infiltration
2. Perivascular cuffing of lymphocytes or polymorphonuclear cells
3. Lymphocytic foci
4. Babes nodules consisting of glial cells
5. Negri bodies

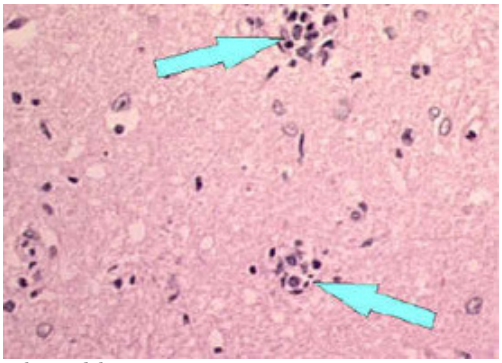


Perivascular cuffing or inflammation around a blood vessel. Perivascular inflammatory cell infiltrates in hematoxylin & eosin stained brain tissue. (100x Magnification)



Perivascular cuffing or inflammation around a blood vessel. Perivascular inflammatory cell infiltrates in hematoxylin & eosin stained brain tissue. (200x Magnification)





Babes Nodules

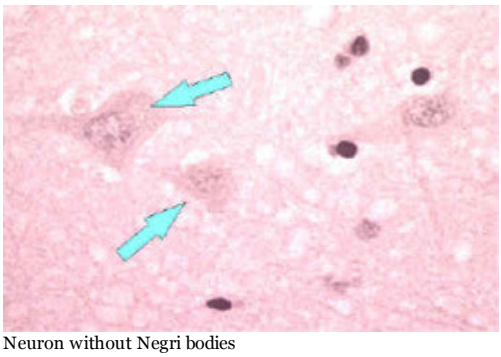
Microscope image of blood vessel without inflammatory cells (Magnified 200x)

Blood vessel without inflamatory cells (200x magnification). A = Red blood cells. B = Squamous epithelial cells

Negri bodies

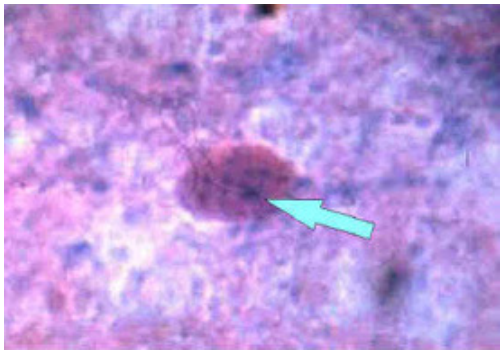
In 1903, most of the histopathologic signs of rabies were recognized, but rabies inclusions had not yet been detected. At this time, Dr. Adelchi Negri reported the identification of what he believed to be the etiologic agent of rabies, the Negri body. In his report, he described Negri bodies as round or oval inclusions within the cytoplasm of nerve cells of animals infected with rabies. Negri bodies may vary in size from 0.25 to 27 µm. They are found most frequently in the pyramidal cells of Ammon's horn, and the Purkinje cells of the cerebellum. They are also found in the cells of the medulla and various other ganglia. Negri bodies can also be found in the neurons of the salivary glands, tongue, or other organs. Staining with Mann's, giemsa, or Sellers stains can permit differentiation of rabies inclusions from other intracellular inclusions. With these stains, Negri bodies appear magenta in color and have small (0.2 µm to 0.5 µm), dark-blue interior basophilic granules.

The presence of Negri bodies is variable. Histologic staining for Negri bodies is neither as sensitive nor as specific as other tests. Some experimentally-infected cases of rabies display Negri bodies in brain tissue; others do not. Histologic examination of tissues from clinically rabid animals show Negri bodies in about 50% of the samples; in contrast, the dFA test shows rabies antigen in nearly 100% of the samples. In other cases, non-rabid tissues have shown inclusions indistinquishable from Negri bodies. Because of these problems, the presence of Negri bodies should not be considered diagnostic for rabies.



Neuron without Negri bodies

Negri body in infected neuron



Enlargement of a Negri body in Sellers stained brain tissue. Note the basophilic (dark blue granules in the inclusion).

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